UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,701	09/24/2001	David M. Mann	CI-0008	4294

34610 7590 06/25/2004

FLESHNER & KIM, LLP
P.O. BOX 221200
CHANTILLY, VA 20153

EXAMINER	
MCKANE, ELIZABETH L	

ART UNIT	PAPER NUMBER
1744	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,701	MANN ET AL.	
	Examiner	Art Unit	
	Leigh McKane	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *103-223* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *140-157* is/are allowed.

6)☒ Claim(s) *103-139 and 157-223* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *092903* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 135 and 139 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

When 135 and 139 depend from claim 104, the claims are vague and indefinite. Claim 104 may limit the claim to irradiation at a reduced temperature. However, both of claim 135 and 139 recite irradiation at an elevated temperature.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 103, 104, 107, 129, and 131-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horowitz et al (U.S. Patent No. 5,981,163) in view of Wiesehahn et al (U.S. Patent No. 4,727,027).

Horowitz et al teaches the sterilization of biological materials, including blood products, wherein the material is treated with a sensitizer and a stabilizer mixture (antioxidant and free-radical scavenger) and irradiated with gamma radiation. The stabilizer mixture may include

flavanoids, such as rutin and quercetin (col.7, lines 5-6). The biological material may be immunoglobulins (col.5, lines 66-67). Moreover, as Horowitz et al discloses the sterilization of a variety of blood products, cells, proteins, and biological fluids and the subsequent use of those materials to treat humans, it would have been obvious to one of ordinary skill in the art to sterilize any biological material intended for use in the treatment of disease. Horowitz et al is silent with respect to adding a ligand to the biological material before irradiation.

Wiesehahn et al teaches a method of sterilizing blood products wherein a stabilizing ligand, heparin, is added to the material before irradiation. Wiesehahn et al discloses that the addition of heparin controls "any activated clotting factors" (col.11, lines 31-33). For this reason, it would have been obvious to add heparin to the blood products being sterilized in the method of Horowitz et al.

5. Claims 109-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horowitz et al and Wiesehahn et al, as applied to claim 103, and further in view of Kent (U.S. Patent No. 6,171,549).

Horowitz et al does not disclose controlling the dose rate of applied radiation. However, Kent, teaches that when sterilizing sensitive biological materials with gamma radiation, one should choose a low dose rate (0.1-3.0 kGy/hr). See Abstract. As this dose rate is disclosed by Kent to be effective in sterilizing without undue damage to the biological material, it would have been obvious to use in the method of Horowitz et al.

6. Claims 103-108 and 118-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson (U.S. Patent No. 5,730,933) in view of Horowitz et al and Wiesehahn et al.

Peterson teaches the use of e-beam or gamma radiation to sterilize a biological material that is sensitive to radiation, wherein a stabilizer (antioxidant/free-radical scavenger, such as ascorbate or propyl galate) is added to the material prior to irradiation and the material is then irradiated "under standard sterilization conditions...at an intensity and for a time duration sufficient to destroy substantially all of the microorganism contamination" (col.4, lines 59-64). See also col.4, lines 36-51; col.6, lines 1-18. The material may also be lyophilized or dried with drying agents and/or frozen and placed under a vacuum or inert gas, such as nitrogen or argon (col.4, lines 51-58; col.5, lines 28-35 and lines 53-67). Peterson does not disclose the use of a flavonoid stabilizer or a ligand stabilizer.

Horowitz et al teaches radiation sterilization of sensitive biological materials wherein a stabilizer mixture including flavanoids, such as rutin and quercetin (col.7, lines 5-6), is used to "quench" both free radicals and reactive forms of oxygen. For this reason, it would have been obvious to add a flavanoid stabilizer in the method of Peterson. Wiesehahn et al teaches a method of sterilizing blood products wherein a stabilizing ligand, heparin, is added to the material before irradiation. Wiesehahn et al discloses that the addition of heparin to a biological material controls "any activated clotting factors" (col.11, lines 31-33). For this reason, it would have been obvious to add heparin to the blood and blood-containing products being sterilized in the method of Peterson.

Peterson does not teach adding a sensitizer to the material prior to irradiation. Horowitz et al, however, teaches a method of sterilizing sensitive biological materials wherein a sensitizer is preferably added prior to irradiation. See Abstract; col.3, lines 34-39, lines 45-47, lines 60-62. As the sensitizer combined with radiation is disclosed to kill viruses without undue damage to

the valuable biological material, it would have been an obvious addition to the method of Peterson.

Moreover, although Peterson fails to teach removal of an organic solvent from the biological material, Horowitz et al discloses that it was known in the art to combine the treatment of a biological material with irradiation and a stabilizer mixture with a second virucidal treatment such as, treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 8. As such merely improves the virucidal effectiveness of the method of Peterson it would have been obvious to first treat the biological material with the organic solvent, followed by removal prior to irradiation.

7. Claims 109-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson, Horowitz et al and Wiesehahn et al, as applied to claim 103, and further in view of Kent (U.S. Patent No. 6,171,549).

Peterson does not disclose controlling the dose rate of applied radiation. However, Kent, teaches that when sterilizing sensitive biological materials with gamma radiation, one should choose a low dose rate (0.1-3.0 kGy/hr). See Abstract. As this dose rate is disclosed by Kent to be effective in sterilizing without undue damage to the biological material, it would have been obvious to use in the method of Peterson.

8. Claims 103, 113-117, and 139 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odland (U.S. Patent No. 5,989,498) in view of Horowitz et al and Wiesehahn et al.

Odland teaches the sterilization of sensitive biological materials at ambient temperature to slightly above ambient (col.4, lines 35-37 and 48-51) with e-beam radiation. Prior to radiation, the biological material is stabilized (cross-linked) with a stabilizer mixture (cross-

linking agents). See col.7, lines 38-58. The material is then irradiated with e-beam radiation at a dose rate of 2.2×10^4 kGy/hr (col.3, line 24). Odland is silent with respect to adding a flavonoid stabilizer and a ligand stabilizer to the material prior to irradiation.

Horowitz et al teaches radiation sterilization of sensitive biological materials wherein a stabilizer mixture including flavanoids, such as rutin and quercetin (col.7, lines 5-6), is used to "quench" both free radicals and reactive forms of oxygen. For this reason, it would have been obvious to add a flavanoid stabilizer in the method of Odland.

Wiesehahn et al teaches a method of sterilizing blood products wherein a stabilizing ligand, heparin, is added to the material before irradiation. Wiesehahn et al discloses that the addition of heparin to a biological material controls "any activated clotting factors" (col.11, lines 31-33). For this reason, it would have been obvious to add heparin to the blood and blood-containing products being sterilized in the method of Odland.

9. Claim 158 is rejected under 35 U.S.C. 103(a) as being unpatentable over Odland in view of Horowitz et al.

Odland teaches the sterilization of sensitive biological materials (heart valves, tissues, etc.) at ambient temperature to slightly above ambient (col.4, lines 35-37 and 48-51) with e-beam radiation. Prior to radiation, the biological material is stabilized (cross-linked) with a stabilizer mixture (cross-linking agents) and the pH is adjusted. See col.7, lines 4-19 and lines 38-58. The material is then irradiated with e-beam radiation at a dose rate of 2.2×10^4 kGy/hr (col.3, line 24). After sterilization the tissues are more pliable, have a greater range of movement, and have an increased durability over non-irradiated tissues. See col.8, lines 47-51. Odland is silent with respect to adding a flavonoid stabilizer to the tissue prior to irradiation.

Horowitz et al teaches radiation sterilization of sensitive biological materials wherein a stabilizer mixture including flavanoids, such as rutin and quercetin (col.7, lines 5-6), is used to "quench" both free radicals and reactive forms of oxygen. For this reason, it would have been obvious to add a flavanoid stabilizer in the method of Odland.

10. Claims 158-166 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson in view of Horowitz et al.

Peterson teaches the use of e-beam or gamma radiation to sterilize a biological material that is sensitive to radiation, wherein a stabilizer (antioxidant/free-radical scavenger, such as ascorbate or propyl galate) is added to the material prior to irradiation and the material is then irradiated "under standard sterilization conditions...at an intensity and for a time duration sufficient to destroy substantially all of the microorganism contamination" (col.4, lines 59-64). See also col.4, lines 36-51; col.6, lines 1-18. The material may also be lyophilized or dried with drying agents and/or frozen and placed under a vacuum or inert gas, such as nitrogen or argon (col.4, lines 51-58; col.5, lines 28-35 and lines 53-67). Peterson does not disclose the use of a flavonoid stabilizer.

Horowitz et al teaches radiation sterilization of sensitive biological materials wherein a stabilizer mixture including flavanoids, such as rutin and quercetin (col.7, lines 5-6), is used to "quench" both free radicals and reactive forms of oxygen. For this reason, it would have been obvious to add a flavanoid stabilizer in the method of Peterson.

As to the recitation "wherein the recovery of the desired activity of the biological material after sterilization by irradiation is greater than 100% of the pre-irradiation value," it is submitted

that this is the natural outcome of the above sterilization process and would have been achieved by the method of Peterson with Horowitz et al..

11. Claims 158-166 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horowitz et al (U.S. Patent No. 5,981,163) in view of Kent et al.

Horowitz et al teaches the sterilization of biological materials, including blood products, wherein the material is treated with a sensitizer and a stabilizer mixture (antioxidant and free-radical scavenger) and irradiated with gamma radiation. The stabilizer mixture may include flavanoids, such as rutin and quercetin (col.7, lines 5-6). The biological material may be immunoglobulins (col.5, lines 66-67). Moreover, as Horowitz et al discloses the sterilization of a variety of blood products, cells, proteins, and biological fluids and the subsequent use of those materials to treat humans, it would have been obvious to one of ordinary skill in the art to sterilize any biological material intended for use in the treatment of disease. Horowitz et al does not disclose controlling the dose rate of applied radiation.

However, Kent, teaches that when sterilizing sensitive biological materials with gamma radiation, one should choose a low dose rate (0.1-3.0 kGy/hr). See Abstract. As this dose rate is disclosed by Kent to be effective in sterilizing without undue damage to the biological material, it would have been obvious to use in the method of Horowitz et al.

As to the recitation "wherein the recovery of the desired activity of the biological material after sterilization by irradiation is greater than 100% of the pre-irradiation value," it is submitted that this is the natural outcome of the above sterilization process and would have been achieved by the method of Peterson with Horowitz et al..

New Matter

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 167-223 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the specification does not provide sufficient support for the limitation in claim 167 of "said effective dose rate is not constant and comprises a rate of between 0.1 kGy/hr to 3.0 kGy/hr for at least a portion of said period of time and a rate of at least 6.0 kGy/hr for at least another portion of said period of time."

Although, as Applicant points out, these limitations were allowed in U.S. Patent No. 6,682,695, the Examiner notes that the limitations in questions were present in original claims 1 and 2 of the above patent, and thus had support in the original disclosure.

Allowable Subject Matter

14. Claims 140-157 are allowed.

Response to Arguments

15. Applicant's arguments with respect to claims 103-139 and 158-166 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh McKane whose telephone number is 571-272-1275. The examiner can normally be reached on Monday-Wednesday (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 571-272-1275. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leigh McKane

Leigh McKane
Primary Examiner
Art Unit 1744

elm
23 June 2004